

AD 59. The vector of claim 1, wherein said heterologous DNA has at least 80% sequence similarity to a gene endogenous to a plant. B

60. The vector of claim 1, wherein said heterologous DNA has at least 90% sequence similarity to a gene endogenous to a plant. C

61. The vector of claim 1, wherein said heterologous DNA has at least 95% sequence similarity to a gene endogenous to a plant.

Remarks

Claims 1-6, 8, 9, 11-16, 18, 19, 21, 31, 32 and 36-61 are pending in this application. Claims 22-30 have been canceled as drawn to a non-elected invention. Claims 7, 10, 17, 20, 33 and 34 have been canceled for the purposes of rewriting. Claims 36-60 have been added. Claims 1, 4-6, 8, 9, 11, 12, 16, 18, 19, 21 and 31 have been amended, as discussed below. Applicants provide attached hereto copies of the "Amendments to the Specification With Revisions Shown" and "Claim Amendments With Revisions Shown," which indicate the nature of the present amendments.

The amendments to the specification and claims, as well as the outstanding rejections, will be addressed below.

I. Amendments to the Specification and Claims.

The specification has been amended at page 10, lines 3-7, has been amended herein to recite: "As used herein, an 'endogenous' plant gene refers to a gene integrated into the chromosomal DNA of the plant genome [gene]." Applicants submit that this amendment is to correct an obvious typographical error in the application as filed and therefore presents no new matter.

The independent claims and Claims 8, 9, 18 and 19 have been amended to recite "at least 60%" sequence similarity. This amendment is supported by the application at page 11, lines 1-3. New Claims 36, 38, 40, 42, 44, 46, 48, 50,

52, 54 and 56 also include this recitation. New Claims 59-61 more specifically recite at least 80%, 90% or 95% sequence similarity. These claims are supported by the application at page 11, lines 3-6.

Independent Claims 1 and 12 have been amended to recite that the endogenous plant gene "occurs naturally in the plant genome." This amendment is supported by the application as filed at page 10, lines 3-7, which recites:

As used herein, an "endogenous" plant gene refers to a gene integrated into the chromosomal DNA of the plant genome. Endogenous genes include those that occur naturally in the plant genome, as well as those artificially introduced (such as by *Agrobacterium*-mediated transformation or ballistic bombardment).

This claim language is also found in new dependent Claims 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, and 57.

Independent Claim 1 has been amended to recite that "said geminivirus silencing vector silences expression of the endogenous plant gene upon introduction into a plant cell." This amendment is supported by the preamble of the claim and throughout the specification as filed. New Claims 36, 38, 42 and 44 also contain this recitation.

Claims 4 and 5 have been amended to correct a typographical error and to provide proper antecedent basis.

Claims 6 and 16 have been amended to correct obvious typographical errors.

Claim 11 has been amended to recite "wherein expression of said heterologous DNA modifies a plant phenotypic trait." New Claim 58 more specifically recites that the plant phenotypic trait "can be visually observed." The amendment to Claim 11 and new Claim 58 are supported by the specification, which states:

The gene silencing may resulted in an altered phenotype; "altered phenotype" as used herein includes alterations in characteristics that can be visually observed (e.g., color), measured (e.g., average height or other growth characteristics) or biochemically assessed (e.g., presence of amounts of target gene products, including RNA, protein or peptide products, or downstream biochemical pathway products).

(Specification; page 9 line 27 to page 10 line 2).

Claims 18, 19 and 21 have been amended to correct a typographical error and to provide proper antecedent basis.

Claim 31 has been amended to delete dependency from canceled base claims. Claim 31 has also been amended to delete the dependency from Claim 12, which lacks proper antecedent basis.

New Claim 36 recites a geminivirus silencing vector comprising a heterologous DNA that is has "at least 60% sequence similarity to a fragment of a gene endogenous to a plant, wherein the heterologous DNA is inserted into the silencing vector in the sense orientation." This amendment is supported throughout the specification as filed, *see e.g.*, originally filed Claims 6 and 8.

New Claim 38 is essentially a rewriting of canceled Claim 7 in independent form.

New Claim 40 is essentially a rewriting of canceled Claim 17 in independent form.

New Claims 42, 44, 46 and 48 are essentially a rewriting of canceled Claims 10 and 20 in independent form.

New Claims 50, 52, 54 and 56 are essentially a rewriting of canceled Claims 33 and 34 in independent form.

In view of the foregoing, Applicants submit that the amendments to the claims and specification submitted herein present no new matter, and respectfully request entry thereof.

II. Written Description.

Claims 1-21 and 31-34 stand rejected under 35 U.S.C. § 112, first paragraph for lack of written description. This rejection is respectfully traversed below.

As an initial matter, Applicants note that the U.S.P.T.O. has recently clarified the standard for examining applications for compliance with respect

to the written description requirement of 35 U.S.C. §112, first paragraph.

These guidelines state, in part:

The examiner has the initial burden, after a thorough reading and evaluation of the content of the application, of presenting evidence or reasons why a person skilled in the art would not recognize that the written description of the invention provides support for the claims. There is a strong presumption that an adequate written description of the claimed invention is present in the specification as filed Consequently, rejection of an original claim for lack of written description should be rare.

(Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, first paragraph, "Written Description" Requirement, 66 Fed. Reg. 1099, 1105 (Jan. 5, 2001); emphasis added).

The outstanding rejection does not satisfy the burden set out above to conclude there is a lack of written support. Moreover, the present claims do not present one of the "rare" instances in which rejection of an originally presented claim for lack of written support is appropriate.

The Office Action states that

[T]he specification provides adequate description for the construction and use of a geminivirus based vector capable of silencing two genes in *N. benthamiana*: the methyl transferase gene and a transgene, luciferase. . . . The claimed invention encompasses sequences capable of silencing any and all genes in any and all plants. The inventors provide specific sequences used for silencing the *N. benthamiana* methyl transferase gene and transgenic luciferase gene, but no direction is given as to identify what sequences in other genes are claimed as capable of silencing said genes.

(Office Action, page 3, second paragraph). Applicants respectfully disagree.

As a preliminary matter, Applicants note that the present application demonstrates silencing of the magnesium chelatase gene, and not the methyltransferase gene. Further, the outstanding rejection provides no objective evidence as to why one skilled in the art would not find that the inventors had possession of the claimed invention in view of the disclosure in the specification. For example, the Examiner states that Applicants have only disclosed actual reduction to practice in tobacco using a plant gene and a transgene, but

provides no evidence or reasoning as to why one skilled in the art would doubt that Applicants were also in possession of gene silencing vectors and methods for use in other species of plants and with other gene silencing constructs. Indeed, as discussed below with respect to the enablement rejection, Applicants have also reduced the invention to practice in *N. benthamiana* and *Arabidopsis* using the plant cellular nuclear antigen (PCNA) gene, the phytoene desaturase gene, and the green fluorescent protein transgene.

Moreover, in contrast to the assertions in the outstanding rejection, the present specification gives extensive guidance as to what other gene sequences and what other plants may be used to carry out the present invention. The present application describes the characteristics of DNA silencing episomes according to the present invention (e.g., page 9, line 19 to page 10, line 2 and page 10, line 26 to page 11, line 6 and page 13, lines 7-27). The degree of sequence similarity to effect gene silencing is described (e.g., page 10, line 31 to page 11, line 6). The heterologous sequence used to effect gene silencing may be in the sense or anti-sense orientation, may be frame-shifted, and may share sequence similarity with all or only part of the endogenous plant gene (e.g., page 11, lines 12-15 and Examples). Methods of gene silencing (page 14, line 22 to page 16, line 16 and Examples) and plants (page 16, line 22 to page 17, line 18) are also described.

Accordingly, it would be apparent to one skilled in the art that Applicants were in possession of the claimed invention.

Finally, the Office Action states that Claims 1 and 12 encompass "sequences with 1% homology to an 'endogenous gene.'" Applicants respectfully note that the claims have been amended to recite at least a 60% (or higher) sequence similarity between the heterologous sequence carried by the silencing vector and the endogenous plant gene to be silenced.

In view of the foregoing, Applicants respectfully submit that the claims are supported by the written description in the application as filed, and request that the outstanding rejection under 35 U.S.C. § 112, first paragraph be withdrawn.

III. Enablement.

Claims 31-34 stand rejected as non-enabled, the Examiner stating that the "specification, while being enabling for the silencing of the methyl transferase gene and the luciferase gene in *N. Benthamiana*, does not reasonably provide enablement for the silencing of any and all genes in any and all plant species." (Office Action, page 4, final paragraph).

The "test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation." (MPEP §2164.01, citing *In re Wands*, 858 F.2d 731, 737). With respect to the present application, the Examiner has acknowledged that the claims are enabled with respect to *N. Benthamiana*, the magnesium chelatase gene, and the luciferase transgene, but has questioned enablement with respect to silencing vectors and methods in other plants or using other genes. The Examiner has provided no objective evidence to doubt the veracity of Applicants' specification, or that the invention does not work as described. The Patent Office has the affirmative burden to set forth such evidence in order to establish even a *prima facie* case of non-enablement (MPEP § 2164.04; *In re Wright*, 999 F.2d 1557 (Fed. Cir. 1993); *In re Marzocchi*, 439 F.2d 220, 224 (CCPA 1971)). Thus, the rejection should be withdrawn.

As described in the preceding section, the application provides substantial guidance as to how the invention may be carried out with other genes and other plant species.

The Office Action expresses concern that Applicants have not demonstrated actual reduction to practice using plants other than tobacco and genes other than magnesium chelatase and luciferase. Applicants note that disclosure in the specification of an actual reduction to practice is *not* necessary to satisfy the enablement requirement (see, MPEP §2164.02; *Gould v. Quigg*, 822 F.2d 1074, 1078; 3 USPQ 2d 1302, 1304 (Fed. Cir. 1987)).

The Office Action concedes that: "Gene silencing in plants as a phenomenon has long been recognized. Silencing has been shown to occur in endogenous genes, transgenes and viral genes." (Office Action, page 5, lines 1-2). Thus, the Examiner acknowledges that gene silencing is known to occur with a wide variety of genes expressed in plants. No objective reasoning has been presented as to why silencing of these various types of genes cannot be effected using the vectors and methods of the invention.

Nonetheless, enclosed herewith is a manuscript by C. Peele et al. (accepted by *The Plant Journal*) describing additional gene silencing results in *N. Benthamiana* using a TGMV silencing vector expressing fragments of the proliferating cell nuclear antigen (PCNA) gene.

Also enclosed is a manuscript by M. Turnage et al. demonstrating gene silencing in *Arabidopsis* using a cabbage leaf curl virus (CLCV) silencing vector. This manuscript reports silencing using CLCV silencing vectors of the magnesium chelatase and phytoene desaturase genes, and a green fluorescent protein transgene, in *Arabidopsis*.

These results demonstrate actual reduction to practice of the present invention in (1) another plant species that is distantly related to *N. benthamiana*; (2) using a geminivirus silencing vector that is distantly related to TGMV; and (3) in two additional naturally-occurring plant genes and one additional transgene.

The Office Action cites the Covey et al. reference regarding the state of the art with respect to the mechanism of gene silencing. Applicants respectfully note that patentability does not require an understanding of the molecular basis of the invention. Similar comments are applicable to the cited statement from Kjemtrup et al. While this reference states that the mechanism of action by which episomal DNA effects gene silencing in plants is incompletely understood, it does not cast doubt as to whether gene silencing may be achieved using a wide variety of vectors, episomal sequences and plant species.

The Examiner further states that the Neuhaber et al. reference provides evidence regarding the unpredictability of gene silencing. The Examiner notes that Neuhaber et al. concerns an integrated homologous sequence, rather than an episome, "however, it is possible that the forms of silencing share commonalities. The fact that transgene silencing is incompletely predictable reflects upon the level of confidence involved in episomally mediated gene silencing." (Office Action, page 5, lines 17-20; emphasis added). Applicants respectfully note that it is not necessary that the invention be completely predictable to satisfy the enablement requirement. Moreover, the relevance of the Neuhaber studies are questionable since this reference was particularly concerned with position effects of the integrated sequences.

Finally, the Office Action states that Atkinson suggests that there is a correlation between episomal copy number and the degree of silencing. Applicants submit that this finding is not surprising and does not suggest that the present invention is non-enabled. It is only required that the specification teach one skilled in the art how to make and use the claimed invention. The issue is not whether some experimentation is necessary to optimize the invention; the relevant question is whether the amount of experimentation is "undue."

Assuming, *arguendo*, that there are some genes or some plant species in which gene silencing according to the present invention is not observed, Applicants respectfully note that MPEP §2164.08(b) provides that the existence of inoperative embodiments within the scope of a claim does not necessarily render a claim non-enabled. The standard is whether a skilled person could determine which embodiments that were conceived, but not yet made, would be inoperative or operative with the expenditure of no more effort than is normally required in the art.

Moreover, the Court of Appeals for the Federal Circuit has held that it is not necessary for the specification or claims to list all operative embodiments, or to exclude all inoperative embodiments, stating: "Even if some of the

claimed combinations [are] inoperative, the claims are not necessarily invalid. 'It is not a function of the claims to specifically exclude ... possible inoperative substances...'. *Atlas Powder Co. v. DuPont*, 750 F.2d 1569; 224 USPQ 409 (CAFC 1984). All that is required by § 112 is that one skilled in the art may determine the inoperative embodiments with no more than routine skill. Applicants submit that this standard is satisfied in the present application.

Applicants note that gene silencing is known in the art. The application provides guidance as to the desired properties of the geminivirus silencing vectors according to the present invention. The application further provides extensive guidance as to how to select the heterologous DNA sequence to effect gene silencing, as well as how to produce and deliver the silencing vector. The present claims are enabled as one skilled in the art could follow the numerous teachings in the specification to carry out the invention throughout the scope of the claims, including embodiments employing different plant species and different plant genes to be silenced. See *In re Strahilevitz*, 668 F2d 1229; 212 USPQ 561 (CCPA 1982).

Applicants have presented evidence of actual reduction to practice in *N. benthamiana* using two plant genes and one transgene. It is possible that there are some embodiments of the invention that are inoperative, but these may be determined with no more than routine experimentation. Accordingly, Applicants submit that the present claims are enabled.

Finally, Claim 32 recites a "plant comprising a plurality of plant cells according to claim 31." This claim stands rejected as non-enabled on the basis that:

Plurality in this context can mean two or several cells. These cells could be widely distributed in the plant. The claims as a whole are drawn to silencing genes in a plant. It is questioned whether down regulating one gene in several cells widely distributed in a plant constitutes silencing. Hence, the silencing of a gene in a plurality of cells does not enable the claim of silencing genes in a plant.

(Office Action, page 6, final paragraph).

Applicants are somewhat unclear as to the basis of this rejection. Claim 32 is a composition claim to a plant that comprises a plurality of plant cells according to Claim 31 (*i.e.*, plant cells comprising a geminivirus silencing vector according to Claim 1). The plant cell of Claim 31 may be an isolated cell, a cell in plant tissue culture, or a cell in a plant, and the like. Claim 32 specifically recites that the cells are in a plant. Applicants have actual reduction to practice of the subject matter of Claim 32 in the Examples and the enclosed manuscript. Claim 32 is not a method claim, and more particularly, is not drawn to a method of silencing a gene in every cell in a plant. Applicants note for the record that silencing with geminivirus vectors is routinely observed in contiguous cells, *see, e.g.*, Kjemtrup et al. at page 98, col. 1, lines 5-8 ("Because microprojectile bombardment targets only a few cells, but the silenced area comprises several hundred cells, we suspect that a diffusible factor may be involved.")

In view of the foregoing discussion, Applicants respectfully submit that the subject matter of the pending claims is enabled, and respectfully request that the outstanding rejection on this basis be withdrawn.

IV. Rejections under 35 U.S.C. § 112, second paragraph.

Claims 1-21 and 33-34 stand rejected on various grounds of indefiniteness under 35 U.S.C. § 112, second paragraph. The individual rejections will be addressed below.

A. Claim 1.

Claim 1 stands rejected as indefinite as "an incomplete claim," on the basis that the body of the claim does not "substantiate" the recitation of a "geminivirus silencing vector" in the preamble of the claim. Applicants note that Claim 1 is a composition claim and does recite the features of the inventive silencing vector. Nonetheless, to expedite the prosecution of the present application in accordance with the USPTO Patent Business Goals (65 Fed. Reg. 54603, September 8, 2000), Claim 1 has been amended to recite "wherein said geminivirus silencing vector silences expression of the endogenous plant gene

upon introduction into a plant cell." This recitation is also found in new Claims 36, 38, 42 and 44. Applicants respectfully submit that this amendment to Claim 1 clarifies that the vector recited by the body of the claim is in accord with the preamble. Applicants further respectfully submit that this claim amendment is not a narrowing amendment as the claim already recited that the vector was a "silencing vector."

In view of the foregoing, Applicants submit that Claim 1 particularly points out and distinctly claims the subject matter of the present invention, and respectfully request that the outstanding rejection under § 112, second paragraph be withdrawn.

B. "Substantial."

Claims 1-21 and 31-34 stand rejected for indefiniteness on the basis of the recitation of "substantial" in Claims 1, 8, 9, 12, 18 and 19, which the Examiner states is a relative term and unclear. Applicants note that the use of "substantial" or "substantially" is accepted practice by the USPTO (see, MPEP § 2173.05 (b)). Moreover, the present application defines a sequence that has "substantial sequence similarity to a gene endogenous to a plant" (see, Specification, page 10, line 31 to page 11, line 6). Nonetheless, to expedite the prosecution of the present application in accordance with the USPTO Patent Business Goals, Claims 1, 8, 9, 12, 18 and 19 have been amended to recite "at least 60% sequence homology." This amendment is supported by the application at page 11, lines 1-3. New Claims 36, 38, 40, 42, 44, 46, 48, 50, 52, 54 and 56 also include this recitation. New Claims 59-61 more specifically recite at least 80%, 90% or 95% sequence similarity. These claims are supported by the application at page 11, lines 3-6.

In view of the foregoing, it is respectfully submitted that the outstanding rejection has been obviated. Accordingly, Applicants request that the outstanding indefiniteness rejection be withdrawn.

C. "Heterologous DNA."

Claims 1-21 and 31-34 stand rejected for indefiniteness on the basis that the recitation of a "heterologous" DNA is unclear. The Examiner states that the term "heterologous" is a "relative term which renders the claim indefinite." This rejection is traversed below.

Applicants note that the MPEP states that the claims need only "define the patentable subject matter with a reasonable degree of particularity and distinctness." (MPEP 2173.02). The specification defines the term "heterologous DNA sequence" as a "recombinant" sequence (page 10, line 29). The application further states that "the term 'heterologous DNA' contained on the DNA silencing episome refers to DNA that is not naturally found in conjunction with the DNA episomal construct, i.e., that has been introduced by genetic engineering techniques" (Specification, page 11, lines 7-10). Thus, a "heterologous" DNA sequence according to the invention is one that is foreign to the silencing construct (e.g., foreign to the geminivirus) and has been introduced into the construct using genetic manipulation. For example, a geminivirus silencing construct may carry a heterologous sequence that is a sense or antisense sequence from a plant gene encoding an enzyme. This usage of the term "heterologous" is both common and accepted in the art and in U.S. patent practice.

In view of the foregoing, Applicants respectfully submit that the recitation of "heterologous" in the claims satisfies the standards of §112, paragraph 2. If the Examiner has any remaining concerns, it is respectfully requested that the Examiner suggest appropriate claim language in accordance with MPEP §2173.02.

D. "Observable."

Claim 11 stands rejected on the basis that the recitation of "observable" renders the claim indefinite. The Examiner states that a "phenotypic trait can be the color of a plant. It also might mean the transcription of an RNA molecule or the translation of a protein molecule. The applicants do not provide guidance as

to what they consider an observable trait and therefore the claim is rendered vague and indefinite." (Office Action, page 9, final paragraph). This rejection is addressed below.

Claim 11 has been amended to recite that "expression of said heterologous DNA modifies a plant phenotypic trait." Applicants note that this is a broadening amendment. New Claim 58 more specifically recites that the plant phenotypic trait "can be visually observed." The amendment to Claim 11 and new Claim 58 are supported by the specification, which states:

The gene silencing may resulted in an altered phenotype; "altered phenotype" as used herein includes alterations in characteristics that can be visually observed (e.g., color), measured (e.g., average height or other growth characteristics) or biochemically assessed (e.g., presence of amounts of target gene products, including RNA, protein or peptide products, or downstream biochemical pathway products).

(Specification; page 9 line 27 to page 10 line 2).

Thus, Claim 11 is drawn to methods in which a phenotypic trait is altered, whereas Claim 58 is more specifically drawn to methods wherein the phenotypic trait is one that can be "visually observed," as defined by the specification. These terms would be clear to those of ordinary skill in the art based on the claim language, common usage in the art, and the specification.

In view of the foregoing, it is submitted that Claim 11 (and new Claim 58) particularly point out and distinctly claim the present invention. Accordingly, it is respectfully requested that the outstanding rejection under § 112, second paragraph be withdrawn.

E. "Endogenous."

Claims 1-21 and 31-34 stand rejected on the basis that recitation of an "endogenous" plant gene (or "gene endogenous to a plant") renders the claims indefinite. In particular, the Examiner states that the "commonly accepted definition for an endogenous gene is a gene which naturally occurs in a plant, i.e. the gene has not been introduced by means of laboratory transformation

techniques" (Office Action, page 10, final paragraph). This rejection is respectfully addressed below.

The application states that:

As used herein, an "endogenous" plant gene refers to a gene integrated into the chromosomal DNA of the plant genome. Endogenous genes include those that occur naturally in the plant genome, as well as those artificially introduced (such as by *Agrobacterium*-mediated transformation or ballistic bombardment).

(Specification, page 10, lines 3-7; corrected by amendment herein).

Applicants agree that one commonly accepted meaning of the term "endogenous" would be a naturally occurring plant gene. Applicants submit, however, that the use of the word "endogenous" to also include foreign sequences that are integrated into the plant genome would not be "repugnant to the usual meaning of that term," particularly in light of the clear guidance in the specification regarding the meaning of this term.

Applicants again note that the MPEP cautions that the Examiner "should allow claims which define the patentable subject matter with a reasonable degree of particularity and distinctness." (MPEP § 2173.02). Further, the Applicants respectfully request that the Examiner suggest alternative claim language if there are remaining concerns regarding the present claims in accordance with MPEP §2173.02.

In view of the foregoing, Applicants submit that the recitation of "endogenous" is clear and respectfully request withdrawal of the outstanding rejection for indefiniteness.

Finally, Applicants note that Claims 1 and 12 have been amended to recite "a gene endogenous to a plant that occurs naturally in the plant genome." New Claims 37, 39, 41, 43, 45, 47, 49, 51, 53, 55 and 57 likewise recite "said gene endogenous to a plant occurs naturally in the plant genome."

F. Antecedent Basis for Claims 4, 5 and 17-21.

Claims 4 and 5 stand rejected for indefiniteness on the basis of lack of antecedent basis for the term "DNA construct." Claims 4 and 5 have been

amended herein to recite a "vector," which has proper antecedent basis in Claim 1.

Claims 17-21 stand rejected for indefiniteness on the basis of lack of proper antecedent basis for the term "vector." Claims 17 and 20 have been canceled for the purposes of rewriting. Claims 18, 19 and 21 have been amended to recite a "DNA construct," which has proper antecedent basis in the base claim.

Applicants respectfully submit that the foregoing claim amendments have addressed the outstanding rejections, and respectfully request that the rejection under § 112, paragraph 2 be withdrawn.

The Office Action further states that "since it is not inferred that claim 12 involves an in vivo use for the DNA construct, this claim does not encompass any use regarding the silencing of genes." Applicants note that Claim 12, and dependents, are drawn to compositions and not methods; accordingly, Applicants find it unnecessary at this time to respond to the Examiner's comments. This lack of response in no way constitutes an acceptance or acquiescence to the Examiner's characterization of the subject matter of Claim 12 and dependents.

V. The Claims are Novel over the Art.

Claims 1-9, 11-16, 18, 19, 21, 31 and 32 stand rejected under 35 U.S.C. § 102 (b) as anticipated by Matzeit et al. Applicants note with appreciation that Claims 10, 17, 20, 33 and 34 are free of the outstanding anticipation rejection and the art of record. If the Examiner maintains the present rejection, Applicants respectfully request that the Examiner clarify the nature of the outstanding rejection in view of the Examiner's discussion of Hayes et al., Fromm et al., Paszkowski et al., and Stanley et al. in addition to the Matzeit et al. reference.

Matzeit et al. describe an expression vector in which the viral coat protein is replaced by a full-length coding sequence for one of three different

bacterial marker proteins (neomycin phosphotransferase, chloramphenicol acetyltransferase, or β -galactosidase).

With respect to Claims 1-6, 8, 9, 11, 31, 32, 36-39, 42-45 and 58-60, which specifically recite "silencing vector," Matzeit et al. only discloses a geminivirus expression vector containing a full-length coding sequence expressing a bacterial protein. Matzeit et al. does not disclose or suggest a silencing vector that "silences expression of the endogenous plant gene upon introduction into a plant cell," as recited by Claims 1-6, 8, 9, 11, 31, 32, 36-39, 42-45 and 58-61.

Moreover, Claims 1 and 12 have been amended to recite a heterologous DNA "having at least 60% sequence similarity to a gene endogenous to a plant that occurs naturally in the plant genome." As Matzeit et al. only discloses heterologous sequences encoding bacterial proteins, the amendments to Claims 1 and 12 obviate the outstanding rejection with respect to these claims as well as dependent Claims 2-6, 8, 9, 11, 13-16, 18, 19, 21, 31, 32 and 58-61.

New Claims 36 and 37 recite a geminivirus silencing vector wherein the heterologous sequence is in the sense orientation and further wherein the heterologous sequence has "at least 60% sequence similarity to a fragment of a gene endogenous to a plant." Matzeit et al. does not disclose a geminivirus vector comprising a less than full-length sequence in the sense orientation. Moreover, one of ordinary skill in the art would have no motivation with respect to the silencing vector of Claim 36 from the Matzeit reference. There would have been no suggestion to one of ordinary skill to construct a silencing vector comprising a less than full-length sequence in the sense orientation based on the expression constructs of Matzeit et al. Matzeit et al. teaches expression constructs for expressing a full-length coding sequence encoding a functional bacterial enzyme; there would have been no motivation to express a less than full-length sequence for the purpose of silencing gene expression.

New Claims 38-39 particularly recite a silencing vector comprising an antisense sequence. Matzeit et al. is only concerned with full-length sense constructs encoding bacterial enzymes. The Matzeit et al. reference provides no disclosure or suggestion regarding a geminivirus silencing vector comprising an antisense sequence.

Likewise, new Claim 40 recites a DNA construct comprising an antisense sequence. Claim 40 is a rewriting of Claim 17 in independent form. As Claim 17 is free of the rejection over Matzeit et al., Applicants submit that new Claim 40 (and dependent Claim 41) is free of the outstanding rejection as well.

New Claims 42 and 46 specifically recite Tomato Golden Mosaic Virus, and new Claims 44 and 48 specifically recite African Cassava Mosaic Virus. Claims 42, 44, 46 and 48 are a rewriting of Claims 10 and 20 in independent form. As Claims 10 and 20 are free of the rejection over Matzeit et al., Applicants submit that new Claims 42, 44, 46 and 48 (and dependent Claims 43, 45, 47 and 49) are free of the outstanding rejection as well.

New Claims 50, 52, 54 and 56 recite methods of silencing the expression of a gene in a plant cell or a plant. Claims 50, 52, 54 and 56 are a rewriting of Claims 33 and 34 in independent form. As Claims 33 and 34 are free of the rejection over Matzeit et al., Applicants submit that new Claims 50, 52, 54 and 56 (and dependent Claims 51, 53, 55 and 57) are free of the outstanding rejection as well.

The Examiner also discusses a reference by Hayes et al., although as indicated above it is not clear whether these references are being relied upon to reject the present claims. Similar to Matzeit et al., Hayes et al. discloses a TGMV expression vector expressing a full-length bacterial neomycin phosphotransferase gene (Abstract). Applicants submit that the subject matter of the pending claims is novel over this reference for the reasons set forth above with respect to Matzeit et al.

The Examiner further discusses references by Paszkowski et al., Fromm et al., and Stanley et al. Paszkowski et al. discloses a "mosaic"

marker gene for use in "studies of RNA splicing, DNA recombination and early events after infection of plants with *Agrobacterium*." (Abstract). Fromm et al. discloses methods of stable transformation of maize using electroporation. As such, Applicants submit that these references clearly do not disclose or suggest the presently-claimed invention.

Finally, the Office Action states on page 14 that Claims 1-9, 11-16, 18, 19, 21, 31 and 32 are anticipated by Stanley et al. The Office Action also states that "[i]n particular, Stanley's constructs clearly anticipate Claim 10." Applicants again respectfully request that if the Examiner maintains the present rejection, the Examiner clarify whether the claims are rejected over Stanley et al. and, more specifically, which claims are rejected.

Stanley et al. describes a pseudorecombinant experiments in which the genomic components of the Nigerian and Kenyan isolates of the cassava latent virus (CLV) are co-inoculated (e.g., genome A from Kenyan isolate and genome B from Nigerian isolate). Stanley et al. reported that the physical properties of the coat protein correlate with genome A, and that some systemic determinants correlate with genome A.

The Examiner states that Stanley et al. "discloses the construction of pseudorecombinant African cassava mosaic viruses in which the coat protein of the Kenyan and Nigerian isolates have been exchanged. Within the scope of the definition of 'heterologous DNA' and 'endogenous gene' used by applicant" (Office Action, page 14, lines 1-5; citation omitted). Applicants disagree with this conclusion and respectfully submit that the studies in the Stanley et al. reference have been misconstrued. Stanley et al. does not demonstrate introduction of a foreign sequence into the CLV coat protein. Stanley et al. used the intact genomic A and B components; this publication reports the results of experiments in which homologous versus heterologous A/B genomes from two different strains of CLV were co-inoculated. It was concluded that the properties of the coat protein correlate with genome A, and that some symptom determinants correlate with genome A.

Applicants submit that the subject matter of the pending claims is novel over this reference for the reasons set forth above with respect to Matzeit et al. For example, the Stanley et al. publication does not disclose or suggest a geminivirus "silencing vector" that "silences expression of the endogenous plant gene upon introduction into a plant cell" as recited by Claims 1-6, 8, 9, 11, 31, 32, 36-39, 42-45 and 58-61. Moreover, Stanley et al. does not disclose or suggest a silencing vector or DNA construct comprising a heterologous sequence that has "at least 60% sequence similarity to a gene endogenous to a plant that occurs naturally in the plant genome" (or higher degree of sequence similarity) as recited by Claims 1-6, 8, 9, 11, 13-16, 18, 19, 21, 31, 32 and 58-61. Likewise, Stanley et al. does not disclose or suggest a silencing vector or DNA construct comprising a heterologous sequence that is in the sense orientation and has sequence similarity to a less than full length portion of an endogenous plant gene (as recited by Claims 36 and 37) or a heterologous sequence that is in the antisense orientation (as recited by Claims 38-41).

Further, as the Office Action indicates that Claims 17, 20, 33 and 34 are free of Stanley et al., new Claims 40, 42, 46, 50, 52, 54 and 56 (and dependents 41, 43, 47, 51, 53, 55 and 57) are also free of this reference, as these claims are a rewriting of canceled Claims 17, 20, 33 and 34 in independent form.

In view of the foregoing, Applicants submit that the subject matter of Claims 1-6, 8, 9, 11-16, 18-21, 31, 32 and 36-60 is novel and nonobvious over the cited Matzeit et al. reference, and respectfully request that the outstanding anticipation rejection be withdrawn.

VI. Conclusions.

The points and concerns raised by the Examiner in the outstanding Office Action having been addressed in full, it is respectfully submitted that this application is in condition for allowance, which action is respectfully requested. Should the Examiner have any remaining concerns, it is

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respectfully requested that the Examiner contact the undersigned attorney to expedite the prosecution of this application to allowance.



Respectfully submitted,

Karen A. Magri
Registration No. 41,965

Enclosure: Peele et al. manuscript
Turnage et al. manuscript

Customer Number:



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PATENT TRADEMARK OFFICE

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to Commissioner for Patents, Washington, DC 20231, on July 16, 2001.

Michele P. McMahan

Date of Signature: July 16, 2001

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Amendments to the Specification With Revisions Shown

Please make the following amendments to the specification at page 10, lines 3-7:

As used herein, an "endogenous" plant gene refers to a gene integrated into the chromosomal DNA of the plant genome [gene]. Endogenous genes include those that occur naturally in the plant genome, as well as those artificially introduced (such as by *Agrobacterium*-mediated transformation or ballistic bombardment).

Claim Amendments With Revisions Shown

1. (Amended) A geminivirus silencing vector comprising a geminivirus genome which contains heterologous DNA, said heterologous DNA having at least 60% [substantial] sequence similarity to a gene endogenous to a plant that occurs naturally in the plant genome, wherein said geminivirus silencing vector silences expression of the endogenous plant gene upon introduction into a plant cell.

4. (Amended) A vector [DNA construct] according to claim 3, wherein said promoter is the promoter that is associated with said endogenous plant gene.

5. (Amended) A vector [DNA construct] according to claim 3, wherein said promoter is the geminivirus coat protein promoter.

6. (Amended) A vector according to claim 1, wherein said heterologous DNA is in the sense orientation.

8. (Amended) A vector according to claim 1, wherein said heterologous DNA has at least 60% [substantial] sequence similarity to a fragment of said endogenous plant gene.

9. A vector according to claim 1, wherein said heterologous DNA has at least 60% [substantial] sequence similarity to the entire coding region of endogenous plant gene.

11. (Amended) The vector of claim 1, wherein expression of said heterologous DNA modifies a [observable] plant phenotypic trait.

12. (Amended) A DNA construct comprising a geminivirus genome, wherein the DNA encoding the geminivirus coat protein has been replaced in part or in total with heterologous DNA having at least 60% [substantial] sequence similarity to an endogenous plant gene that occurs naturally in the plant genome.

16. (Amended) A DNA construct according to claim 12, wherein said heterologous DNA is in the sense orientation.

18. (Amended) A DNA construct [vector] according to claim 12, wherein said heterologous DNA has at least 60% [substantial] sequence similarity to a fragment of said endogenous plant gene.

19. (Amended) A DNA construct [vector] according to claim 12, wherein said heterologous DNA has at least 60% [substantial] sequence similarity to the entire coding region of said endogenous plant gene.

21. (Amended) The DNA construct [vector] of claim 12, wherein expression of said heterologous DNA modifies an observable plant phenotypic trait.

31. (Amended) A plant cell comprising a geminivirus silencing vector according to claim 1[, 12, 22, 23 or 24].
